

## REMARKS

Claims 1-4, 7-8, 11, and 14-67 are pending in this application for the Examiner's review and consideration. Applicants appreciate the Examiner's allowance of claims 3, 11, 14-16, 18, 33, 34, 45, 46, 53, and 54. New claim 68 is similar to claim 1 but specifically recites the alkyl substituents and aryl substituents disclosed in the specification at page 4, lines 14-31 and page 5, lines 9-18, respectively. Applicants also appreciate the courtesies extended by Examiner Kifle to Applicants' attorneys, Anthony M. Insogna and Paul E. Dietze, in a telephonic interview conducted on July 10, 2002, wherein the Examiner agreed that claim language in related epothilone cases, in particular application no. 09/280,191 ("the '191 application"), would be applicable to this application and that in an interview on July 21, 2001 in the '191 application he agreed to allow, and in fact did allow, composition claims, similar to those in the above-identified matter, that used the term "substituted."<sup>1</sup> No new matter is added by the new claim so that its entry at this time is warranted.

## THE REJECTION UNDER 35 U.S.C. §112 SHOULD BE WITHDRAWN

Claims 1, 2, 4, 7, 8, 17, 19-32, 35-44, 47-52, and 55-67 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the reasons set forth on page 2 of the Office Action. Applicants respectfully traverse the rejection.

The Examiner alleges that the term "substituted" without saying which substituents are intended is indefinite. Applicants respectfully traverse.

"Whether a claim is . . . [indefinite] depends on whether those skilled in the art would understand the scope of the claim when the claim is read in the light of the specification." *North American Vaccine v. American Cyanamid Co.*, 7 F.3d 1571, 1579, 28 U.S.P.Q.2d 1333, 1339 (Fed. Cir. 1993). Second, claims are interpreted in light of the specification and not in a vacuum, as the Examiner appears to be doing. *See, e.g., Exxon Research and Engineering Co. v. U.S.*, 265 F.3d, 1371, 1375 (Fed. Cir. 2001) ("If one skilled in the art would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112, paragraph 2"); *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1478, 45 USPQ 2d, 1429, 1433 (Fed. Cir. 1998) ("The best source for understanding a technical term is the specification from which it arose."); and

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<sup>1</sup> Applicants note, however, that the '191 application has not yet issued as a patent since Applicants filed a Request for Continued Examination ("RCE") and a Supplemental Information Disclosure Statement.

*Standard Oil Co. v. American Cyanamid Co.* 774 F.2d 448, 452, 227 USPQ 293, 296 (Fed. Cir. 1985) ("The descriptive part of the specification aids in ascertaining the scope and meaning of the claims inasmuch as the words of the claims must be based upon the description. The specification is, thus, the primary basis for construing the claims."). In the instant application the specification clearly provides a definition for the term "substituted." The phrases "substituted alkyl" and "substituted aryl" are both clearly defined in the specification as a finite, definitive genus (*See, e.g.*, Specification, page 4, lines 14-30 and page 5, lines 9-18, respectively). Thus, Applicants submit that the claims are clear and not indefinite.

Furthermore, as noted in our previous amendments, a large number of decisions have interpreted claims in light of the specification and held that terms like "substituted alkyl" and "substituted aryl" are not indefinite under 35 U.S.C. § 112, second paragraph. For example, in *Ex parte Lewis et al.*, 197 U.S.P.Q. 543 (Bd. Pat. App. & Inter. 1977), the claim term "substituted alkyl" was found definite. Similarly, in *Ex parte Breuer*, 1 U.S.P.Q.2d 1906 (Bd. Pat. App. & Inter. 1986) the claim terms "substituted aryl" and "substituted alkyl" were found definite (*Cf. Ex parte Takeyama et al.*, 2000 WL 33149253 (Bd. Pat. App. & Inter. 2000)). Accordingly, contrary to the Examiner's allegations, one of ordinary skill in the art, reading the specification, would readily be able to say what is "the metes and bounds of the [claimed] compound" (*See, e.g.*, Office Action, page 2).

The Examiner, further, alleges that the term "substituted" would include toxic heavy metals, dimers with another epothilone, sugars, nucleotides, antibodies, etc. (*See, e.g.*, Office Action, page 2). Applicants respectfully traverse. As noted above, the specification clearly defines the phrases "substituted alkyl" and "substituted aryl" as a finite, definitive genus (*See, e.g.*, Specification, page 4, lines 14-30 and page 5, lines 9-18, respectively). Although, many other moieties could have been recited in the specification as substituents, they were not. These other moieties were not recited since it did not make chemical or biological sense to include these other moieties as substituents on an epothilone molecule. One of ordinary skill in the art, reading the specification, would readily understand the metes and bounds of the term "substituted" and would readily understand the term "substituted" does not include substituents such as toxic moieties.

Moreover, even if some of the substituents recited in the genus disclosed in the specification were inoperable, the mere inclusion of some inoperable species within the genus would not render the claims indefinite. *See, e.g.*, *Exxon Research and Engineering Co.*, at 1382 ("there is nothing indefinite about claim language in this case simply because it covers some embodiments that may be inoperable"); *North American Vaccine v. American Cyanamid Co.*, at 1579 ("The fact that dependent claims include species which might not meet the objectives of the invention does not by

itself prove that one skilled in the art cannot ascertain the scope of the asserted claims"); and *Application of Angstadt*, 537, F.2d, 498, 504, 190 USPQ 214, 219 (CCPA 1976) ("nobody will use them [inoperative embodiments] and the claims do not cover them").

Applicants respectfully submit that the metes and bounds of the term "substituted," when read in light of the specification, would be readily be understood by one of ordinary skill in the art. Accordingly, claims 1, 2, 4, 7, 8, 17, 19-32, 35-44, 47-52, and 55-67 are not indefinite. For the above reasons, Applicants respectfully request that the rejection of claims 1, 2, 4, 7, 8, 17, 19-32, 35-44, 47-52, and 55-67 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

#### CONCLUSION

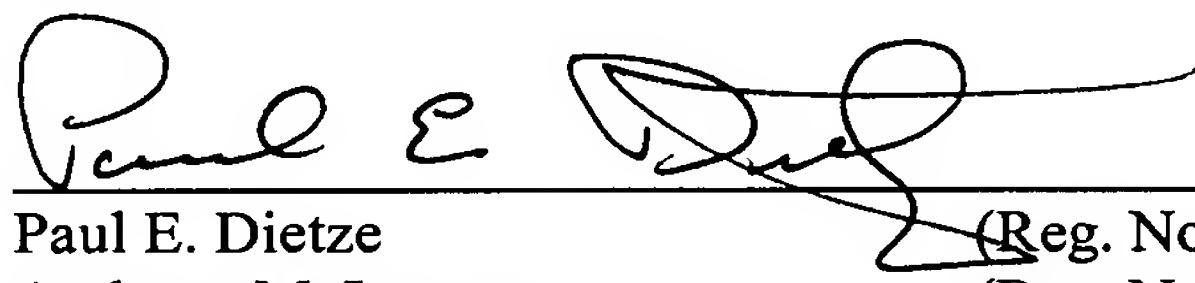
Applicants believe the application is in condition for allowance and earnestly requests reconsideration of the claims and allowance thereof. If the Examiner has any questions or suggestions to expedite allowance of this application, however, the Examiner is respectfully invited to call the undersigned to discuss the matter further.

No amendment fee is believed to be due for this submission. Should any fees be due, however, please charge the fees to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: December 17, 2002

For:

  
Paul E. Dietze  
Anthony M. Insogna

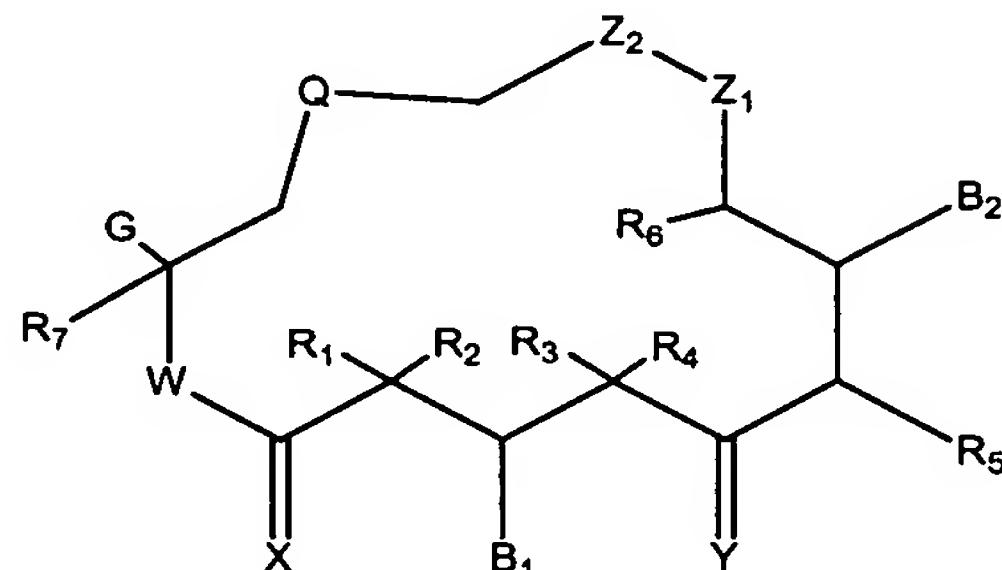
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(Reg. No. 35,203)

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## Appendix A

Pending claims for Application No. 09/084,542; filed May 26, 1998

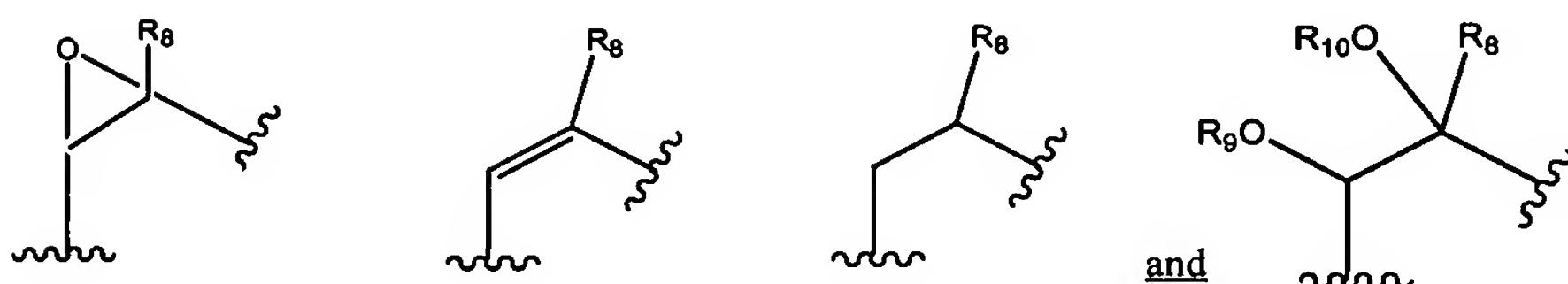
1. A compound of the formula:



V

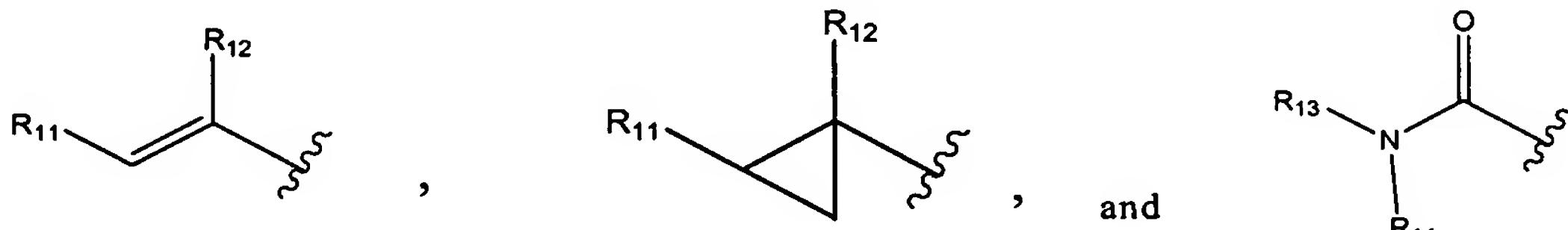
wherein:

Q is selected from the group consisting of:



and

G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



W is O or NR<sub>15</sub>;

X is O or H, H;

Y is selected from the group consisting of O; H, OR<sub>16</sub>; OR<sub>17</sub>, OR<sub>17</sub>; NOR<sub>18</sub>; H, NOR<sub>19</sub>; H, NR<sub>20</sub>R<sub>21</sub>; H, H; and CHR<sub>22</sub>; wherein OR<sub>17</sub>, OR<sub>17</sub> can be a cyclic ketal;

Z<sub>1</sub> and Z<sub>2</sub> are independently CH<sub>2</sub>;

B<sub>1</sub> and B<sub>2</sub> are independently selected from the group consisting of OR<sub>24</sub>, OCOR<sub>25</sub>, and

O-C(=O)-NR<sub>26</sub>R<sub>27</sub>, and when B<sub>1</sub> is OH and Y is OH, H, they can form a six-membered ring ketal or acetal;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>26</sub> and R<sub>27</sub> are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R<sub>1</sub> and R<sub>2</sub> are alkyl can be joined to form a cycloalkyl, and when R<sub>3</sub> and R<sub>4</sub> are alkyl can be joined to form a cycloalkyl;

R<sub>6</sub> is methyl;

R<sub>9</sub>, R<sub>10</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>24</sub>, R<sub>25</sub> and R<sub>31</sub> are selected from the group consisting of H, alkyl, and substituted alkyl;

R<sub>11</sub>, R<sub>12</sub>, R<sub>28</sub>, R<sub>30</sub>, R<sub>32</sub>, and R<sub>33</sub> are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C<sub>3</sub>-C<sub>7</sub> carbocyclic ring; and a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

R<sub>8</sub> is hydrogen or methyl;

R<sub>15</sub>, R<sub>23</sub> and R<sub>29</sub> are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C<sub>3</sub>-C<sub>7</sub> carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; R<sub>32</sub>C=O; R<sub>33</sub>SO<sub>2</sub>; hydroxy; O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof;

with the proviso that compounds wherein

W and X are both O; and

R<sub>1</sub>, R<sub>2</sub> and R<sub>7</sub> are H; and

R<sub>3</sub>, R<sub>4</sub> and R<sub>6</sub> are methyl; and

R<sub>8</sub> is H or methyl; and

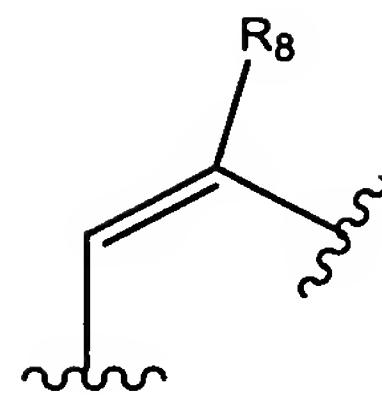
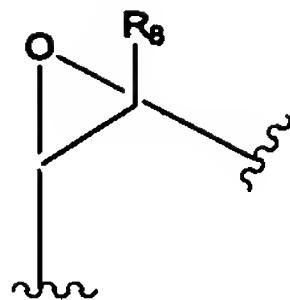
G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and

Q is as defined above

are excluded.

2. The compound of claim 1, wherein

Q is



X is 0;

Y is 0;

Z<sub>1</sub>, and Z<sub>2</sub>, are CH<sub>2</sub> and

W is NR<sub>15</sub>.

3. A compound selected from the group consisting of:

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-4,13,17-trioxabicyclo[4.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-4,13,17-trioxabicyclo[4.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-1,10-dioxa-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-1,10-dioxa-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-4,14,17-trioxabicyclo[4.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,-tetramethyl-3-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-4,14,17-trioxabicyclo[4.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-1,11-dioxa-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1,11-dioxa-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-3,8,8,10,12,16-hexamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-3,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13,16-hexamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,16-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-oxa-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-6,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-4,8,8,10,12,16-hexamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-4,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[4.10]heptadecane-5,9-dione;

[4S-[4R\*-7S\*,8R,\*9R-,15R\*(E)]]-4,8-Dihydroxy-1,5,5,7,9,13-hexamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-1,5,5,7,9-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-10-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,BR\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-10-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-14-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-14-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-11-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,(E)]]-4,8-Dihydroxy,5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl- 4-thiazolyl)ethenyl]-11-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[1S-[1R\*,3R\*,7R\*,10S\*,11R\*,12R\*,16S\*]]-N-Phenyl-7,11-dihydroxy-8,8,10,12,16-pentamethyl- 5,9-dioxo-4,17-dioxabicyclo[14.1.0]heptadecane-3-carboxamide;

[1S-[1R\*,3R\*,7R\*,10S\*,11R\*,12R\*,16S\*]]-N-Phenyl-7,11-dihydroxy-8,8,10,12-tetramethyl-5,9- dioxo-4,17-dioxabicyclo[14.1.0]heptadecane-3-carboxamide;

[4S-[4R\*,7S\*,8R\*,9R\*,15\*]]-N-Phenyl-4,8-dihydroxy-5,5,7,9,13-pentamethyl-2,6-dioxo-1-oxa-13- cyclohexadecene-16-carboxamide;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*]]-N-Phenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-2,6-dioxo-1-oxa-13- cyclohexadecene-16-carboxamide;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1- methyl-2-(2-methyl- 4-thiazolyl)cyclopropyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R\*,3R\*(E),7R\*,10S\*,11R\*,12R\*,16S\*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl- 2-(2-methyl- 4-thiazolyl)cyclopropyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R\*,7S\*,8R\*,9R\*,15R\*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2- hydroxymethyl-4-thiazolyl)ethenyl]-1-aza-13(Z)-cyclohexadecene-2,6-dione;  
and the pharmaceutically acceptable salts, solvates and hydrates thereof.

4. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer,

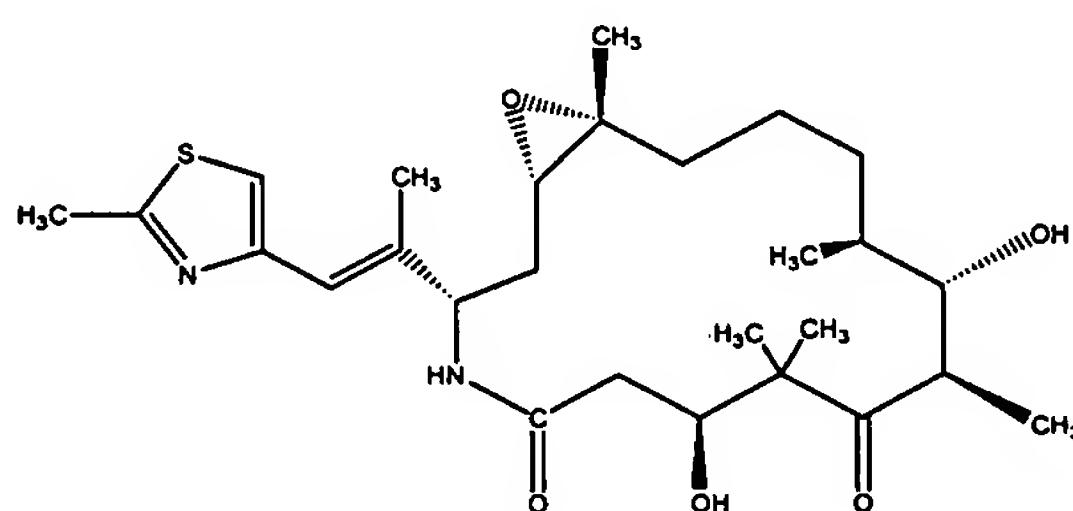
esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

7. The method of claim 4, wherein the cancer is cancer of the breast, ovary, or colon.

8. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

11. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

14. A compound having the formula:



or a pharmaceutically acceptable salt, hydrate, solvate, geometrical isomer, optical isomer or stereoisomer thereof.

15. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said

treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

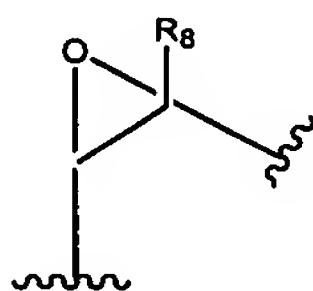
16. The method of claim 15, wherein the cancer is cancer of the breast, ovary, or colon.

17. The method of claim 8, wherein the cancer is cancer of the breast, ovary, or colon.

18. The method of claim 11, wherein the cancer is cancer of the breast, ovary, or colon.

19. The compound of claim 1, wherein G is 1-methyl-2-(substituted-4-thiazolyl) ethenyl group.

20. The compound of claim 1, wherein Q is



21. The compound of claim 1, wherein W is NR15.

22. The compound of claim 1, wherein X and Y are each O.

23. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

24. The method of claim 23, wherein the cancer is cancer of the breast, ovary, or colon.

25. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

26. The method of claim 25, wherein the cancer is cancer of the breast, ovary, or colon.

27. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

28. The method of claim 27, wherein the cancer is cancer of the breast, ovary, or colon.

29. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

30. The method of claim 29, wherein the cancer is cancer of the breast, ovary, or colon.

31. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

32. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 2.

33. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 3.

34. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 14.

35. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 19.

36. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 20.

37. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 21.

38. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 22.

39. The method of claim 4, further comprising administering one or more of a additional anti-cancer agent.

40. The method of claim 39, wherein the additional anti-cancer agent acts in a phase of the cell cycle other than the G<sub>2</sub>-M phase.

41. The method of claim 40, wherein the additional anti-cancer is a thymidilate synthase inhibitor, a DNA cross linking agent, a topoisomerase I or II inhibitor, a DNA alkylating agent, a ribonuclase reductase inhibitor, a cytotoxic factor, or a growth factor inhibitor.

42. The method of claim 4, further comprising administering radiation therapy.

43. A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable vehicle or diluent.

44. A pharmaceutical composition comprising the compound of claim 2 and a pharmaceutically acceptable vehicle or diluent.

45. A pharmaceutical composition comprising the compound of claim 3 and a pharmaceutically acceptable vehicle or diluent.

46. A pharmaceutical composition comprising the compound of claim 14 and a pharmaceutically acceptable vehicle or diluent.

47. A pharmaceutical composition comprising the compound of claim 19 and a pharmaceutically acceptable vehicle or diluent.

48. A pharmaceutical composition comprising the compound of claim 20 and a pharmaceutically acceptable vehicle or diluent.

49. A pharmaceutical composition comprising the compound of claim 21 and a pharmaceutically acceptable vehicle or diluent.

50. A pharmaceutical composition comprising the compound of claim 22 and a pharmaceutically acceptable vehicle or diluent.

51. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

52. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

53. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

54. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

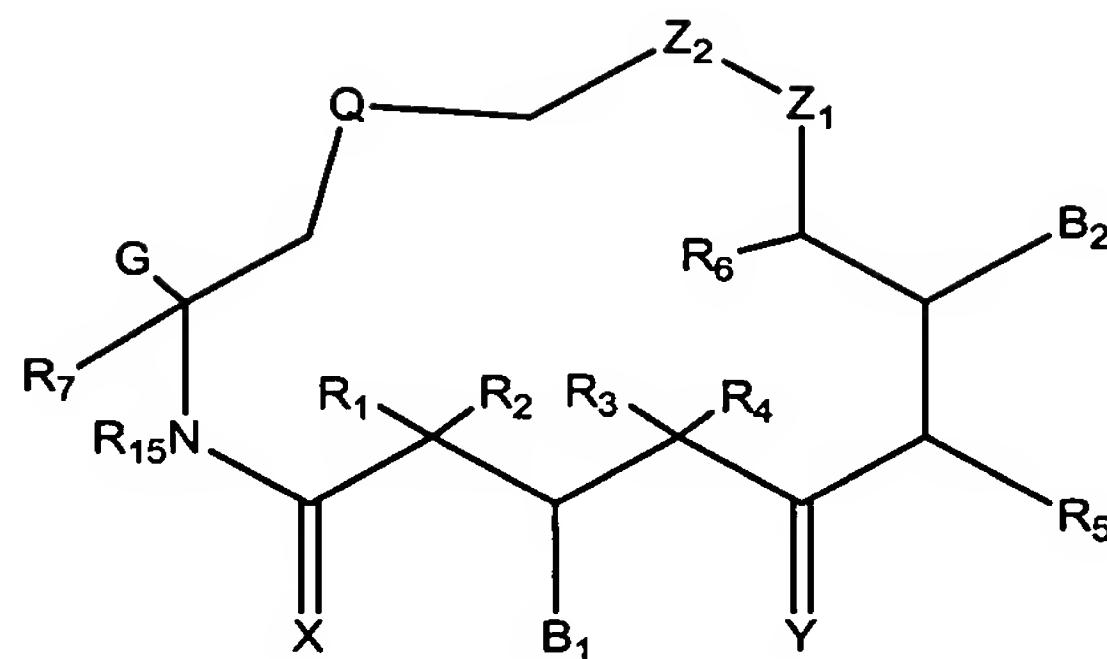
55. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

56. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

57. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

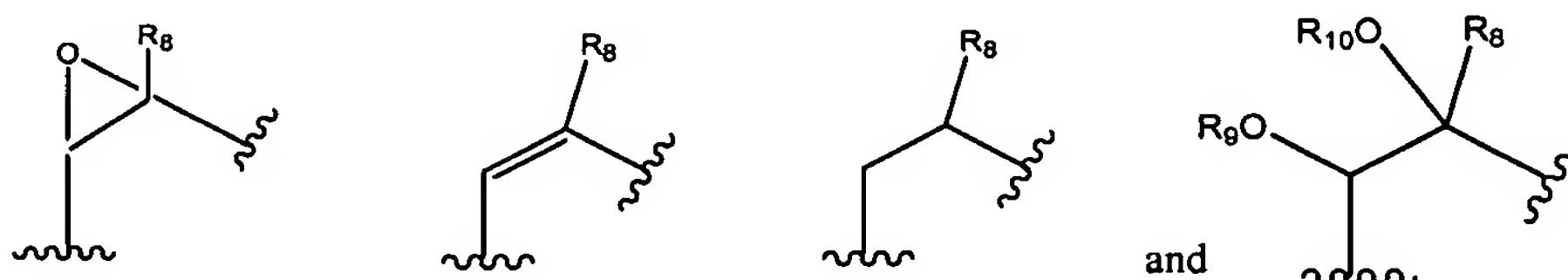
58. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

59. A compound of the formula:

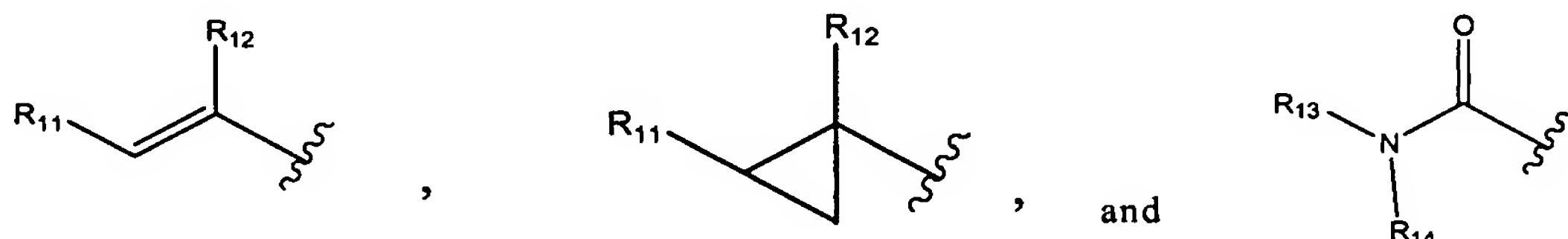


wherein:

Q is selected from the group consisting of:



G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



X is O or H, H;

Y is selected from the group consisting of O; H, OR<sub>16</sub>; OR<sub>17</sub>, OR<sub>17</sub>; NOR<sub>18</sub>; H, NOR<sub>19</sub>; H, NR<sub>20</sub>R<sub>21</sub>; H, H; and CHR<sub>22</sub>; wherein OR<sub>17</sub>, OR<sub>17</sub> can be a cyclic ketal;

Z<sub>1</sub> and Z<sub>2</sub> are independently CH<sub>2</sub>;

B<sub>1</sub> and B<sub>2</sub> are independently selected from the group consisting of OR<sub>24</sub>, OCOR<sub>25</sub>, and O-C(=O)-NR<sub>26</sub>R<sub>27</sub>, and when B<sub>1</sub> is OH and Y is OH, H, they can form a six-membered ring ketal or acetal;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>26</sub> and R<sub>27</sub> are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R<sub>1</sub> and R<sub>2</sub> are alkyl can be joined to form a cycloalkyl, and when R<sub>3</sub> and R<sub>4</sub> are alkyl can be joined to form a cycloalkyl;

$R_6$  is methyl;

$R_9$ ,  $R_{10}$ ,  $R_{16}$ ,  $R_{17}$ ,  $R_{24}$ ,  $R_{25}$  and  $R_{31}$  are selected from the group consisting of H, alkyl, and substituted alkyl;

$R_{11}$ ,  $R_{12}$ ,  $R_{28}$ ,  $R_{30}$ ,  $R_{32}$ , and  $R_{33}$  are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated  $C_3$ - $C_7$  carbocyclic ring; and a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

$R_8$  is hydrogen or methyl;

$R_{15}$ ,  $R_{23}$  and  $R_{29}$  are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated  $C_3$ - $C_7$  carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;  $R_{32}C=O$ ;  $R_{33}SO_2$ ; hydroxy; O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof.

60. A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 59.

61. The method of claim 60, wherein the cancer is cancer of the breast, ovary, or colon.

62. A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 59.

63. The method of claim 60, further comprising administering one or more of a additional anti-cancer agent.

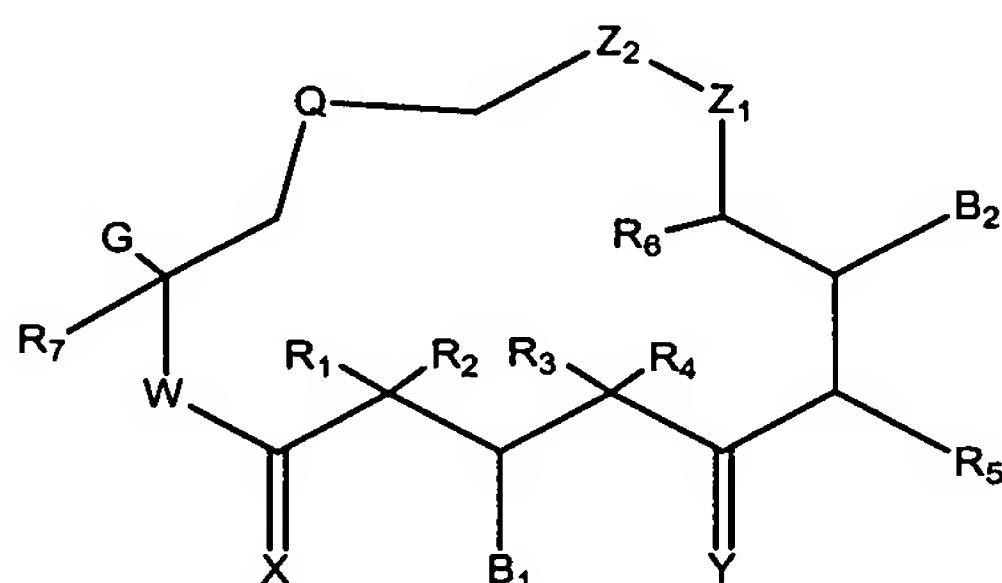
64. The method of claim 63, wherein the additional anti-cancer agent acts in a phase of the cell cycle other than the G<sub>2</sub>-M phase.

65. The method of claim 64, wherein the additional anti-cancer is a thymidilate synthase inhibitor, a DNA cross linking agent, a topoisomerase I or II inhibitor, a DNA alkylating agent, a ribonuclease reductase inhibitor, a cytotoxic factor, or a growth factor inhibitor.

66. A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 59.

67. A pharmaceutical composition comprising the compound of claim 59 and a pharmaceutically acceptable vehicle or diluent.

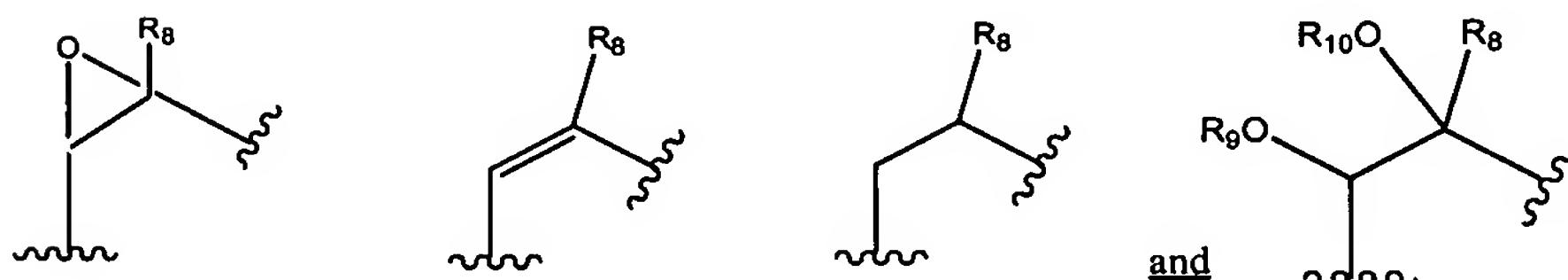
68. (New) A compound of the formula:



V

wherein:

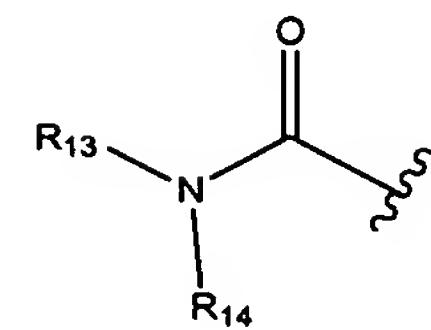
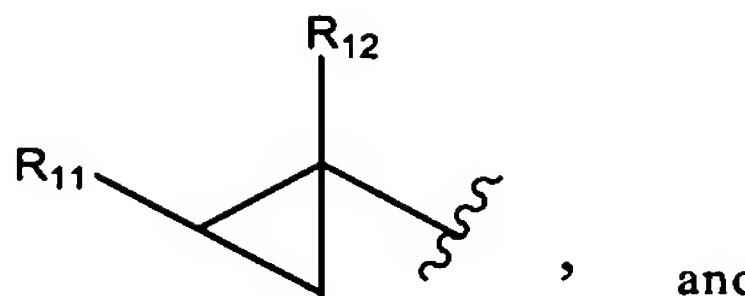
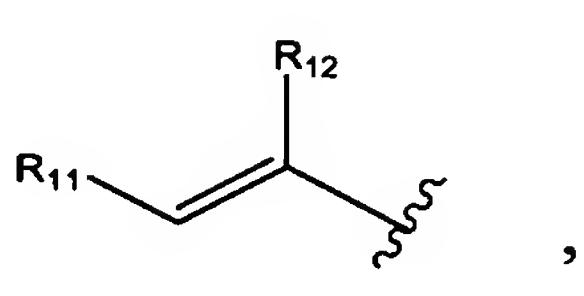
Q is selected from the group consisting of:



and

G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or

unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



W is O or NR<sub>15</sub>;

X is O or H, H;

Y is selected from the group consisting of O; H, OR<sub>16</sub>; OR<sub>17</sub>, OR<sub>17</sub>; NOR<sub>18</sub>; H, NOR<sub>19</sub>; H, NR<sub>20</sub>R<sub>21</sub>; H, H; and CHR<sub>22</sub>; wherein OR<sub>17</sub>, OR<sub>17</sub> can be a cyclic ketal;

Z<sub>1</sub> and Z<sub>2</sub> are independently CH<sub>2</sub>;

B<sub>1</sub> and B<sub>2</sub> are independently selected from the group consisting of OR<sub>24</sub>, OCOR<sub>25</sub>, and O-C(=O)-NR<sub>26</sub>R<sub>27</sub>, and when B<sub>1</sub> is OH and Y is OH, H, they can form a six-membered ring ketal or acetal;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>26</sub> and R<sub>27</sub> are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R<sub>1</sub> and R<sub>2</sub> are alkyl can be joined to form a cycloalkyl, and when R<sub>3</sub> and R<sub>4</sub> are alkyl can be joined to form a cycloalkyl;

R<sub>6</sub> is methyl;

R<sub>9</sub>, R<sub>10</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>24</sub>, R<sub>25</sub> and R<sub>31</sub> are selected from the group consisting of H, alkyl, and substituted alkyl;

R<sub>11</sub>, R<sub>12</sub>, R<sub>28</sub>, R<sub>30</sub>, R<sub>32</sub>, and R<sub>33</sub> are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C<sub>3</sub>-C<sub>7</sub> carbocyclic ring; and a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

R<sub>8</sub> is hydrogen or methyl;

R<sub>15</sub>, R<sub>23</sub> and R<sub>29</sub> are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C<sub>3</sub>-C<sub>7</sub> carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; R<sub>32</sub>C=O; R<sub>33</sub>SO<sub>2</sub>; hydroxy; O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof;

wherein substituted alkyl is an alkyl group substituted with from one to four substituents selected from the group consisting of halo; trifluoromethyl; trifluoromethoxy; hydroxy; alkoxy; cycloalkoxy; heterocyclooxy; oxo; alkanoyl; aryloxy; alkanoyloxy; amino; alkylamino; arylamine; aralkylamino; cycloalkylamino; heterocycloamino; disubstituted amines wherein the substituents are selected from alkyl, aryl, and aralkyl; alkanoylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; arylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; aralkanoylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; thio; alkylthio; aralkylthio; cycloalkylthio; heterocyclothio; alkylthiono; arylthiono; aralkylthiono; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; sulfonamido optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; nitro; cyano; carboxy; carbamyl optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; alkoxycarbonyl; aryl; substituted aryl; guanidino; and heterocyclo; and

substituted aryl is an aryl group substituted with from one to four substituents selected from the group consisting of alkyl; substituted alkyl; halo; trifluoromethyl; trifluoromethoxy; hydroxy; alkoxy; cycloalkoxy; heterocyclooxy; alkanoyl; alkanoyloxy; amino; alkylamino; aralkylamino; cycloalkylamino; heterocycloamino; dialkylamino; alkanoylamino; thio; alkylthio; cycloalkylthio; heterocyclothio; ureido; nitro; cyano; carboxy; carboxyalkyl; carbamyl; alkoxycarbonyl; alkylthiono; arylthiono; alkylsulfonyl; sulfonamido; and aryloxy each of which may be optionally substituted with halo, hydroxy, alkyl, alkoxy, substituted aryl, substituted alkyl, or substituted aralkyl;

with the proviso that compounds wherein

W and X are both O; and

R<sub>1</sub>, R<sub>2</sub> and R<sub>7</sub> are H; and

R<sub>3</sub>, R<sub>4</sub> and R<sub>6</sub> are methyl; and

R<sub>8</sub> is H or methyl; and

G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and

Q is as defined above

are excluded.